REMARKS

The specification is amended to correct obvious typographical and spelling errors and to produce grammatical clarity. The specification is amended to include a claim of priority to U.S. Patent 6,800,728 which is the parent of this divisional application.

The specification is also amended to correct the name of a chemical compound in the paragraph on page 38 line 15. The basis for this amendment is found in the specification, in particular page 38 line 12, which describes the preparation of semicarbazides and thiosemicarbazides.

The specification is also amended to correct a scrivener's error in providing R^{11} instead of R^{10} for the listing of moieties for these variables on page 4 line 6. Support for this can be found in claim 5 wherein only R^{10} is listed as a variable in the moieties defining R and R^{11} is not present.

The specification is also amended by replacing the term "includes" with the word "is" on page 9 line 26, replacing the phrase "include, but not limited to," with the word "maybe" on page 9 line 29, removing the word "including" on page 10 line 8 and line 14 and replacing the word "include" with the word maybe on page 10 line 12 and line 16 as per the Examiner's request.

The specification is also amended to correct an error in the solvent description found in the paragraphs on page 41, line 18 to page 42, line 4. The solvent term "THF" has been replaced with "DMF" in each location it appears. This amendment finds its basis in Figure 3, which shows that the reactions are performed in DMF as the solvent.

The specification is also amended to correct the name of a buffer in the paragraph on page 46, lines 12-23. The basis for this amendment is found in the specification on page 46, lines 16-17, which describes the preparation of a "SANH/PBS" solution.

The specification is also amended to include the phrase "(SEQ ID NO.:1)" after the DNA sequence on page 51 line 30 as requested by the Examiner.

Applicant has amended claim 5 to include "methyl" in the listing of groups for R^1 and R^2. The support for this amendment can be found on page 23 line 16-22.

Applicant has amended claim 6 by replacing the phrase "a saturated or" with "an" to more particularly point out and distinctly claim the subject matter of the instant invention.

Applicant has amended claim 35 and 38 replacing the word "biomolecule" in the second to last line of each claim with "biological molecule" to more particularly point out and distinctly claim the subject matter of the instant invention.

Applicant believes that the amendments to the specification or claims do not add new matter to the specification.

Item 3. The Examiner states that the substitute specification submitted August 31, 2007 was not entered because the marked-up copy of the substitute specification is not identical to the clean copy of the substitute specification. Applicant has reviewed both the marked-up and clean versions of the substitute specifications to assure that they are identical. In particular, the substitute specification terms "$N(COR^{15})$ $N(R^{15})$," has been corrected to read "$N(R^{15})$, $N(COR^{15})$,". Applicant notes that the computer file of the original application submitted in this case could not be obtained from the previous agent of record consequently the entire document had to be recreated. The error noted by the Examiner was merely a typographical error. In addition, the Examiner will note that Example 10 is not amended consequently the implication of new matter is moot.

Item 4. The Examiner states that the amendment to the claims in the response filed August 31, 2007 does not comply with 37 C.F.R. §1.121(c)(1) because a paragraph at the top of this section discussed the absence of claims in the substitute specification. The present amendment excludes this additional paragraph in this section as required under 37 C.F.R. §1.121 (c)(2).
In addition, the Examiner states that claims 5-7, 35 and 38 contained in the response filed August 31, 2007 are improper because they contain and repeat amendment markings from the

amendments made to the claims in the response filed April 16, 2007. Applicant submits herewith amended claims that do not contain or repeat previously accepted amendments from prior responses.

The Examiner further states that the amendments to claim 35 are improper because the phrase "amino or one" has been reinserted into the claim without underlining and the term "biomolecule" has been changed to "biological molecule" without the term biomolecule being striked through. Applicant submits herewith amended claim 35 in the proper format in compliance with 37 C.F.R. 1.121(c)(2), wherein the phrase "amino or one" has not been reinserted and the term "biomolecule" is presented in strike through format or in brackets as required.

The Examiner also states that the amendment to claim 52 is improper because it lists an incorrect status identifier and because it shows "α-bromoacetamide' in strike through when that term was not presented in the pervious version of the claim. Applicant submits herewith claim 52 with the proper identifier "(Previously Amended)" without the second recitation of compound α-bromoacetamide.

Item 5. The Examiner objects to the specification because the term "limited" is misspelled on page 4 line 27 and the terms "SEQ ID NO" was not present after the nucleotide sequence on page 51 line 30. As requested, Applicant has amended the specification with the correct spelling of "limited" and by inserting the phrase "(SEQ ID NO.:1)" after the nucleotide sequence on page 51.

PATENTABILITY ARGUMENTS

A. Response to Rejections under 35 U.S.C. §112 second paragraph

Item 6. The Examiner has rejected claims 5, 6, 35, 38, 49 and 52 under 35 U.S.C. §112 second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. More particularly, the Examiner states that the phrase "a derivative thereof" in claims 5, 32, 35, and 38 are indefinite because it is not clear what degree of structural and/or functional similarity is required to be present in a compound of formula II or Va and a second compound in order for the second compound to be considered a derivative of compounds of formulas II or Va. The Examiner further states that while Applicant's specification describes examples of derivatives the use of the term "includes" obviates such as a definition. Applicant respectfully disagrees. As the Examiner is well aware claims have been, and are, interpreted narrowly regardless of the fact that they are supposed to be afforded reasonable breadth based on the Doctrine of Equivalence. Further Applicant has the right to be his/her own lexicographer and define certain terms to clarify their intended meaning within the scope of the claim language. Particularly when there is no definite art recognized meaning that is contrary to that provided by Applicant. Applicant has provided such a definition on page 9 line 26 through page 10 line 24 as noted by the Examiner. To further clarify Applicant's definition of the phrase "a derivative thereof" he has removed the term "includes" in each place it occurred in this definition. Consequently, the Examiner's rejections are moot and Applicant respectfully requests that this rejection be removed.

Item 7. The Examiner objects to claims 6 and 7 under 37 C.F.R. §1.75(c) as being improper for failing to further limit the subject matter of the previous claim. More particularly the Examiner states the in claim 6, R can be a saturated or unsaturated carbocyclic moiety of 3 to 20 atoms but that claim 5 provides that R is an aliphatic divalent cycloalkylene group. Applicant has amended claim 6 by replacing the phrase "a saturated or" with "an" to be consistent with the term cycloalkylene.

In view of this, the Examiner's rejection is moot and Applicant respectfully requests that the this rejection be removed.

The Examiner then states that claim 5 recites R^1 and R^2 groups as being saturated straight chains of 3 to 20 carbon atoms but claim 7 shows R^1 and R^2 as methyl groups. Claim 5 has been amended to include methyl as a member of the group indicated for R^1 and R^2. In view of this, the Examiner's rejection is moot and Applicant respectfully requests that the this rejection be removed.

B. Response to 35 U.S.C. §102 (b) Rejections

Item 9. The Examiner rejects claims 5-7, 35, 38, 49 and 52 under 35 U.S.C. §102 (b) as being anticipated by WO 01/70865 Applicant's PCT application filed March 22, 2001. The Examiner states that this is available as prior art against the instant claims because of a current lack of an acceptable claim for priority under 35 U.S.C. §120. Applicant has amended the specification to claim the benefit of U.S. patent 6,800,728; application no.: 09/815,978 filed March 22, 2001 which claims priority from provisional patent application serial no.: 60.191,186 filed March 22, 2000. In view of this amendment Applicant's PCT application is no longer properly cited prior art. Applicant respectfully submits that this rejection is now moot and requests that the Examiner remove this rejection.

Item 10. The Examiner has rejected claim 5 under 35 U.S.C. §102(b) as being anticipated by WO patent application 93/14779. He states that examples 5-7 in application '779 teach a compound that is reacted with an arginine derivative and the product is conjugated to the amino group of solid phase resin. This reaction product and the arginine derivative is deemed by the Examiner to be a derivative of Applicant's compound formula II. Applicant respectfully disagrees.

For the Examiner to maintain a rejection under 35 U.S.C. §102(b) every element of Applicant's invention must be taught by the cited reference. The compound of example 5 and the arginine derivative do not have four of the five proscribed elements of formula II. First neither the

compound of example 5 nor that of its arginine derivative have B which is an amino or thiol reactive moiety. These elements are defined on page 18 and 19 of the specification. An "amino reactive moiety" is defined as moieties that react directly with amine moieties forming amide bonds and include N-hydroxysuccinimidyl, p-nitrophenyl, pentafluorophenyl and N-hydroxybenzotriazolyl esters. A thiol reactive group refers to moieties that react directly with sulfhydryl groups forming stable sulfide bonds and include maleimido, α-bromoacetamido and pyridyldisulfides. The compounds of '779 have a –COOH group as B which is not recognized by those skilled in the art as an amino reactive or thiol reactive group. Neither the compound of example 5 nor its arginine derivative have R which is an aliphatic divalent cycloalkylene group. The compounds of '779 have a $-CH_2-(C_6H_{10})$, R group which is not recognized by those skilled in the art as a cycloalkylene. Niether the compounds in example 5 nor its arginine derivative have an R^1 nor and R^2 group which is a saturated straight chain of 3 to 20 carbon atoms, a chain of 2 to 2000 ethyleneoxide moieties, or a saturated or unsaturated carbocyclic moiety of 3 to 20 carbon atoms. Where R^1 and R^2 branch from the carbon of the –N=C< moiety one of the R groups is hydrogen and the other a-(t-butoxycarbonyl)-N^a-nitro argininal group. Consequently, one skilled in the art not recognize either of these as a saturated straight chain of 3 to 20 carbon atoms, a chain of 2 to 2000 ethyleneoxide moieties, or a saturated or unsaturated carbocyclic moiety of 3 to 20 carbon atoms. While it appears that one element, A of the formula –NH-(C=O)- is present in the compound of example 5 and in its arginine derivative this is insufficient to maintain an anticipation rejection under 35 U.S.C. §102 (b). Consequently, the Examiner has not shown, or demonstrated, that '779 teaches every element of Applicant's invention.

In addition, the Examiner suggests that the compounds in Example 5 and their arginine derivatives are identical to the compounds of Applicant's claims because they are deemed to be a derivative under the definition provided in Applicant's specification. Applicant has amended the section of the specification removing the word "includes" from the definition of derivative as requested by the Examiner. In view of this amendment the Examiner cannot claim that the compounds of the Applicant's invention are anticipated by this cited reference. Consequently, Applicant respectfully requests that the Examiner remove this rejection.

Item 11. Next the Examiner rejects claim 5 and 35 as being anticipated by U.S. Patent No.: 6,238,860 to Whelihan. The Examiner states that Whelihan teaches polypeptides which are

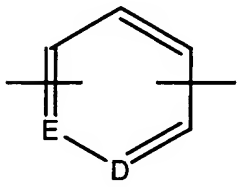
synthesized with a Glu-Gly-Gly-Gly-Ser spacer sequence modified with a hydrazide functionality and then immobilized on an aldehyde functional methacrylate resin support. This polypeptide-spacer-hydrazine reaction product is deemed by the Examiner to be a derivative of Applicant's compound formula II and of Applicant's conjugate of formula Va. Applicant respectfully disagrees.

For the Examiner to maintain a rejection under 35 U.S.C. §102(b) every element of Applicant's invention must be taught by the cited reference. The polypeptide-spacer-hydrazide-reaction product of Whelihan does not have four of the five proscribed elements of formula II. First the reaction product of Whelihan does not have B which is an amino or thiol reactive moiety. These elements are defined on page 18 and 19 of the specification. An "amino reactive moiety" is defined as moieties that react directly with amine moieties forming amide bonds and include N-hydroxysuccinimidyl, p-nitrophenyl, pentafluorophenyl and N-hydroxybenzotriazolyl esters. A thiol reactive group refers to moieties that react directly with sulfhydryl groups forming stable sulfide bonds and include maleimido, a-bromoacetyl, α-bromoacetamido and pyridyldisulfides. The reaction product of Whelihan has a synthetic polypeptide as B which is not recognized by those skilled in the are as an amino reactive or thiol reactive group. Further the reaction product of Whelihan has an amino acid spacer of sequence (-Glu-Gly-Gly-Gly-Ser-) which is not any of the possible aliphatic divalent groups specified in claim 5. In addition, the reaction product does not contain $-N=C(R^1R^2)$ wherein R^1 and R^2 are independently a saturated straight chain of 3 to 20 carbon atoms, a chain of 2 to 2000 ethyleneoxide moieties, or a saturated or unsaturated carbocyclic moiety of 3 to 20 carbon atoms. While it appears that element A, being –NH-(C=O)- may be present in the reaction product this is insufficient to maintain an anticipation rejection under 35 U.S.C. §102 (b). Consequently, the Examiner has not shown, or demonstrated, that Whelihan teaches every element in claim 5 of Applicant's invention.

In addition, the Examiner suggests that the polypeptide-spacer-hydrazine-reaction product is identical to the compounds of Applicant's claims, specifically formula II, because it is deemed to be a derivative under the definition provided in Applicant's specification. Applicant has amended the section of the specification removing the word "includes" from the definition of derivative as requested by the Examiner. In view of this amendment the Examiner cannot claim

that the compounds of the Applicant's invention are anticipated by this cited reference. Consequently, Applicant respectfully requests that the Examiner remove this rejection.

Regarding claim 35, the polypeptide-spacer-hydrazide-reaction product of Whelihan does not have at least two of the five proscribed elements of formula Va. The reaction product does not have the moieties, $-N=C(R^1R^2)$ nor the following structure:



wherein E and D may be C or N. While the reaction product does have B wherein B is a natural or synthetic biological molecule, such as a polypeptide and may have A wherein A is –NH-(C=O)- this is insufficient to maintain an anticipation rejection under 35 U.S.C. §102 (b). Consequently, the Examiner has not shown, or demonstrated, that Whelihan teaches every element in claim 35 of Applicant's invention.

In addition, the Examiner suggests that the polypeptide-spacer-hydrazine-reaction product is identical to the compounds of Applicant's claims, specifically formula Va, because it is deemed to be a derivative under the definition provided in Applicant's specification. Applicant has amended the section of the specification removing the word "includes" from the definition of derivative as requested by the Examiner. In view of this amendment the Examiner cannot claim that the compounds of the Applicant's invention are anticipated by this cited reference. Consequently, Applicant respectfully requests that the Examiner remove this rejection.

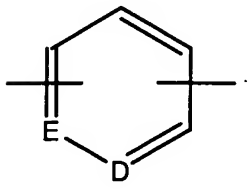
Item 12. Next the Examiner rejects claim 5 and 38 as being anticipated by U.S. Patent No.: 5,521,290 to Sivam *et al.*. The Examiner states that Sivam teaches derivatizing a monoclonal antibody with sulfhydryl groups reacting a hydrazide containing bifunctional linker of formula I with the derivatized monoclonal antibody and then reacting the monoclonal hydrazide with ricin A which has been oxidized to form aldehyde groups on its oligosaccharide moieties. This

derivatized monoclonal antibody and the bifunctional linker is deemed by the Examiner to be Applicant's compound formula II and of Applicant's conjugate of formula Va. Applicant respectfully disagrees.

For the Examiner to maintain a rejection under 35 U.S.C. §102(b) every element of Applicant's invention must be taught by the cited reference. The linker of formula 1 of Sivam does not have three of the five proscribed elements of formula II. First formula 1 does not have have R which is an aliphatic divalent cycloalkylene group. The compounds of Sivam have a $-CH_2-(C_6H_{10})$ R group which is not recognized by those skilled in the art as a cycloalkylene. Further Formula 1 does not contain $-N=C(R^1R^2)$ wherein R^1 and R^2 are independently a saturated straight chain of 3 to 20 carbon atoms, a chain of 2 to 2000 ethyleneoxide moieties, or a saturated or unsaturated carbocyclic moiety of 3 to 20 carbon atoms. While the formula 1 does have B wherein B is a amino reactive or thiol reactive moiety such as a maleimide reactive group and may have A wherein A is –NH-(C=O)- this is insufficient to maintain an anticipation rejection under 35 U.S.C. §102 (b). Consequently, the Examiner has not shown, or demonstrated, that Whelihan teaches every element in claim 35 of Applicant's invention.

In addition, the Examiner suggests that the linker of formula 1 is identical to the compounds of Applicant's claims, specifically formula II, because it is deemed to be a derivative under the definition provided in Applicant's specification. Applicant has amended the section of the specification removing the word "includes" from the definition of derivative as requested by the Examiner. In view of this amendment the Examiner cannot claim that the compounds of the Applicant's invention are anticipated by this cited reference. Consequently, Applicant respectfully requests that the Examiner remove this rejection.

Regarding claim 38, the derivatized monoclonal antibody of Sivam does not have at least two of the five proscribed elements of formula Va. The reaction product does not have $-N=C(R^1R^2)$ nor the following structure:



wherein E and D may be C or N. While the reaction product does have B wherein B is a natural or synthetic biological molecule, such as a monoclonal antibody and may have A wherein A is –NH-(C=O)- this is insufficient to maintain an anticipation rejection under 35 U.S.C. §102 (b). Consequently, the Examiner has not shown, or demonstrated, that Whelihan teaches every element in claim 35 of Applicant's invention.

In addition, the Examiner suggests that the derivatized monoclonal antibody is identical to the compounds of Applicant's claims, specifically formula Va, because it is deemed to be a derivative under the definition provided in Applicant's specification. Applicant has amended the section of the specification removing the word "includes" from the definition of derivative as requested by the Examiner. In view of this amendment the Examiner cannot claim that the compounds of the Applicant's invention are anticipated by this cited reference. Consequently, Applicant respectfully requests that the Examiner remove this rejection.

Item 13. The Examiner maintains his rejection of the claims under 35 U.S.C. §112, second paragraph because he believes that the phrase "a derivative thereof" is indefinite. More specifically, he believes that it is not clear what degree of structural and/or functional similarity is required to be present in a compound of formula II or Va and a second compound in order for the second compound to be considered a derivative of compounds of formulas II or Va. The Examiner further states that while Applicant specification describes examples of derivatives the use of the term "includes" obviates such a definition. Applicant respectfully disagrees and reiterates their response. As the Examiner is well aware Applicant has the right to be his/her own lexicographer and define certain terms to clarify their intended meaning within the scope of the claim language. Particularly when there is no definite art recognized meaning that is contrary to that provided by Applicant. Applicant has provided such a definition on page 9 line 26 through page 10 line 24 as noted by the Examiner. However, in order to comply with the Examiner's

requests the term "includes" in each place it occurred in this definition has been removed. Consequently, the Examiner's rejections are moot and Applicant respectfully requests that this rejection be removed.

In view of this, the rejections based on anticipation in which the Examiner relies solely on his belief that Applicant has not properly defined "a derivative thereof" is moot. Since Applicant has met the requirements under 35 U.S.C. the Examiner's rejections under 35 U.S.C. §102(b) are now improper and moot. Applicant respectfully requests that the Examiner remove these rejections.

In view of the above, Applicant respectfully requests that the Examiner issue an allowance of the claims.

SUMMARY

If the Examiner believes that it would facilitate prosecution, Applicant's agent, David B. Waller, may be contacted at (619) 230-7478, or at dwaller@gordonrees.com.

Please charge any shortage in fees due in connection with the filing of this paper, including extension of time fees, to Deposit Account 50-1990 and please credit any excess fees to such deposit account.

Respectfully submitted,

Dated: 3/17/08

By: _____

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